

**WHAT IS CLAIMED IS:**

1           1.       A method for determining whether a test compound modulates the drug  
2 resistance of a cell, the method comprising:

3               a) determining the level of expression or activity of a resistance sequence in a cell  
4 in the presence of a test compound; ✓

5               b) determining the level of expression or activity of the resistance sequence in the  
6 cell in the absence of the test compound; and

7               c) identifying the compound as a modulator of drug resistance of the cell if the  
8 level of expression or activity of the resistance sequence in the cell in the presence of the test  
9 compound differs from the level of expression of the resistance sequence in the cell in the  
10 absence of the test compound. } no full for "up"

1           2.       The method of claim 1, wherein the resistance sequence is a nucleic acid  
2 encoding a protein selected from the group consisting of semaphorin D, B94, mel-14 antigen,  
3 24p3, proliferin, and maspin.

1           3.       The method of claim 1, wherein the resistance sequence is a polypeptide  
2 selected from the group consisting of semaphorin D, B94, mel-14 antigen, 24p3, proliferin,  
3 and maspin.

1           4.       The method of claim 1 wherein the resistance sequence is encoded by an  
2 endogenous gene.

1           5.       A method for determining whether a test cell has a drug-resistant  
2 phenotype, the method comprising:

3               a) measuring the expression or activity of a resistance sequence in the test cell;

4               b) comparing the expression or activity of the resistance sequence measured in  
5 step a) to the expression or activity of the resistance sequence in a control cell not having a  
6 drug-resistant phenotype; and ✓

7               c) determining that the test cell has a drug resistant phenotype if the expression or  
8 activity of the resistance sequence in the test cell differs compared to the expression or  
9 activity of the resistance sequence in the control cell. ✓

1           6.       The method of claim 5, wherein the resistance sequence is selected from  
2 the group consisting of semaphorin D, B94, mel-14 antigen, 24p3, proliferin, and maspin.

1           7.       A method for determining whether a subject has or is at risk of developing  
2 a drug resistant tumor, the method comprising:

3           a) measuring the expression of an up-regulated or down-regulated resistance  
4 mRNA in a biological sample comprising tumor cells obtained from the subject;

5           b) comparing the expression of the mRNA measured in step a) to the expression  
6 of the mRNA in a control biological sample that is not drug resistant; and

7           c) determining that the patient has or is at risk of developing a drug resistant  
8 tumor if the expression of an up-regulated mRNA in the biological sample obtained from the  
9 patient is higher than the expression of the up-regulated mRNA in the control biological  
10 sample, or decreased expression of a down-regulated mRNA in the biological sample  
11 obtained from the patient is lower than the expression of the down-regulated mRNA in the  
12 control biological sample.

1           8.       A method for treating a drug resistant tumor in a patient, the method  
2 comprising administering to said subject an amount of an up-regulated protein antagonist or a  
3 down-regulated protein agonist effective to reduce drug resistance of said tumor in the  
4 patient.

1           9.       A method for determining whether a drug therapy should be continued in a  
2 patient, the method comprising:

3           a. obtaining a biological sample comprising tumor cells from the patient;

4           b. determining the expression level of a resistance sequence in the patient sample;

5           c. comparing the expression level determined in step (b) with the expression of  
6 the resistance sequence in a drug sensitive biological sample; and

7           d. discontinuing treatment when the expression level of the resistance sequence  
8 in the patient sample is altered compared to the expression of the resistance sequence in the  
9 drug sensitive sample.

1           10.      The method of claim 9, wherein the resistance sequence is an up-regulated  
2 sequence and treatment is discontinued when expression of the sequence is increased  
3 compared to the expression of the sequence in the drug sensitive sample.

1           11.      The method of claim 9, wherein the resistance sequence is a down-  
2 regulated sequence and treatment is discontinued when expression of the sequence is  
3 decreased compared to the expression of the sequence in the drug sensitive sample.

1           12.    A method for determining whether a drug therapy should be continued in a  
2 patient, the method comprising

3           a. obtaining a first patient biological sample comprising tumor cells and a second  
4 biological sample comprising tumor cells, wherein the first sample is obtained prior to the  
5 second sample;

6           b. determining the expression level of a resistance sequence in the second  
7 sample;

8           c. determining the expression level of a resistance sequence in the first sample;

9           c. comparing the expression level of the resistance sequence determined in step  
10 (b) to the expression level of the resistance sequence in step (c); and

11          d. discontinuing treatment when the expression level of the second sample differs  
12 from the expression level of the resistance sequence in the first sample.

1           13.    The method of claim 12, wherein the resistance sequence is an up-  
2 regulated sequence and treatment is discontinued when expression of the sequence in the  
3 second sample is increased compared to the expression of the sequence in the first sample.

1           14.    The method of claim 12, wherein the resistance sequence is a down-  
2 regulated sequence and treatment is discontinued when expression of the sequence in the  
3 second sample is decreased compared to the expression of the sequence in the first sample.

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1           15.    A method for treating a drug resistant tumor in a patient, the method  
2 comprising administering to the patient a compound that reduces the expression of a protein  
3 selected from the group consisting of: semaphorin D, B94, mel-14 antigen, 24p3, and  
4 proliferin.

1           16.    A method for treating a drug resistant tumor in a patient, the method  
2 comprising administering to the patient a compound that reduces the activity of a protein  
3 selected from the group consisting of: semaphorin D, B94, mel-14 antigen, 24p3, and  
4 proliferin.

1           17.    A method for treating a drug resistant tumor in a patient, the method  
2 comprising administering to the patient a compound that increases the expression of maspin.

1 18. A method for treating a drug resistant tumor in a patient, the method  
2 comprising administering to the patient a compound that increases the activity of maspin.

1 19. A method for determining whether a drug therapy should be continued in a  
2 patient, the method comprising

3 a. obtaining a first patient biological sample comprising tumor cells and a second  
4 biological sample comprising tumor cells, wherein the first sample is obtained prior to the  
5 second sample;

6 b. determining the expression level of a gene selected from the group consisting  
7 of: semaphorin D, B94, mel-14 antigen, 24p3, and proliferin in the second sample;

8 c. determining the expression level of the selected gene in the first sample;

9 c. comparing the expression level determined in step (b) to the expression level  
10 determined in step (c); and

11 d. discontinuing treatment when the expression level determined in step (b) is  
12 greater than the expression level determined in step (c).

1 20. A method for determining whether a drug therapy should be continued in a  
2 patient, the method comprising

3 a. obtaining a first patient biological sample comprising tumor cells and a second  
4 biological sample comprising tumor cells, wherein the first sample is obtained prior to the  
5 second sample;

6 b. determining the expression level of maspin in the second sample;

7 c. determining the expression level of maspin in the first sample;

8 c. comparing the expression level determined in step (b) to the expression level  
9 determined in step (c); and

10 d. discontinuing treatment when the expression level determined in step (b) is  
11 less than the expression level determined in step (c).

1 21. The method of claim 19 or 20 wherein the expression level is determined  
2 by measuring mRNA expression.

1 22. The method of claim 19 or 20 wherein the expression level is determined  
2 by measuring protein expression.

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